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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,339	12/21/2001	Vincenzo Cannata	217689US40	4736

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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	6

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,339	CANNATA ET AL.	
	Examin r	Art Unit	
	Cybille Delacroix-Muirheid	1614	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *38-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The following is responsive to Applicant's election received Aug. 8, 2003.

Applicant's election of Group I claims 1-37 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 38-73 are withdrawn from consideration.

Information Disclosure Statement

Applicant's Information Disclosure Statements received June 7, 2002 and Sep. 3, 2002 have been considered. Please refer to Applicant's copies of the 1149 submitted herewith.

PLEASE NOTE: reference AO was not considered because no English abstract was submitted.

Claim Objections

1. Claims 29 and 34 are objected to because of the following informalities: in claim 29, line 1, the term –further—should be added before "comprising". In claim 34, line 1, the term "an" before "acid" should be deleted and replaced with –of a mineral--. Appropriate correction is required.

Claim Rejections—35 USC 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 13-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 13-14 recite the limitation "the mineral acid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections—35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Augart et al., 6,054,482 in view of Satzinger et al., 4,024,175 and Jennings et al., 5,693,845.

Augart et al. disclose a pharmaceutical composition containing gabapentin hydrochloride (i.e. the acid addition salt of gabapentin) in combination with a pharmaceutically acceptable carrier. Augart et al. disclose that the hydrochloride of gabapentin is the most suitable form of the active material since salts, especially hydrochlorides, general provide especially good stability and good solubility. However, in order to keep undesirable lactam content of the composition low (i.e. not exceed 0.5% by weight of gabapentin lactam), and in order to ensure storage stability, Augart et al. teach that the composition should contain a proportion of hydrochloride, which does not exceed 20 ppm. This also applies to other mineral acids. Please see col. 1, lines 10-25; col. 2, lines 12-16; col. 3, lines 62-65; col. 5, lines 18-29, lines 11-17; Example 1.

Augart et al. does not specifically set forth the claimed mineral acids as claimed by Applicant in claim 13, nor do Augart et al. specifically disclose that the proportion of hydrochloride is at most 5 ppm (i.e. 5 ppm's or less), as claimed by Applicant. However, the Examiner refers to (1) Satzinger et al., which disclose that gabapentin can form pharmacologically compatible salts with inorganic and organic acids such as hydrochloric acid, sulfuric acid, phosphoric acid. (please see col. 2, lines 1-5) and (2) Jennings et al., which disclose that pharmaceutical acid addition salts of gabapentin

include salts derived from inorganic acids such as hydrobromic acid, nitric acid, hydroiodic acid and aliphatic sulfonic acids . (please see col. 2, lines 29-31; col. 7, lines 48-56).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the gabapentin hydrochloride composition of Augart et al. to form acid addition salts using the inorganic mineral acids such as those described by Satzinger et al. and Jennings et al. because both Satzinger and Jennings clearly suggest that acid addition salts of gabapentin are pharmaceutically or pharmacologically acceptable, and one of ordinary skill in the art would reasonably expect the resulting compositions to be equally effective in providing therapeutic benefit to patients in need of gabapentin. In other words, such a modification would have been motivated by the reasonable expectation of producing pharmaceutical compositions, which are just as therapeutically effective as gabapentin hydrochloride.

Moreover, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the amount of the acid addition salt to a range of 5 ppm or less because Augart et al. establish that the amount of hydrochloride should not exceed 20 ppm, and one of ordinary skill in the art would reasonably expect a composition containing any amount below 20 ppm (such as the claimed 5 ppm or less) to be equally stable and to not contain more than 0.5% by weight gabepentin lactam. Finally, since Augart et al. establish that stability is dependent upon the amount (ppm) of hydrochloride in the gabapentin composition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the amount

of hydrochloride as well as other acid addition salts such that it is effective to optimize the stability of the overall composition.

With respect to the concentration of water in the composition, it would have been obvious to one of ordinary skill in the art to modify the amount of water in the composition so as to not affect stability of the overall composition.

Finally, concerning claims 10 and 11, since the claimed compositions are substantially similar to the compositions disclosed by Augart et al., Satzinger and Jennings, the undetectable quantities of acid addition salt would be obvious.

5. Claims 19-28, 30-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singer et al., 6,531,509 B2 in view of Satzinger et al., 4,024,175 and Jennings et al., 5,693,845.

Singer et al. disclose stable pharmaceutical compositions containing gabapentin, wherein gabapentin containing composition contains an anion of a mineral acid, such as chloride, in amounts greater than 20 ppm, e.g. 20 ppm, 50 ppm, 100 ppm, 150-200 ppm. Singer et al. additionally disclose that the pharmaceutical compositions can contain pharmaceutically acceptable excipients. Finally, the disclosed compositions when stored for a year at 55 degrees C and at 60% atmospheric humidity contain an amount of gabapentin lactam, which does not exceed 0.2% by weight of the gabapentin. Please see the abstract; col. 2, lines 50-67; col. 3, lines 22-34; Example 14, Example 2, Example 10, Table 2; claim 5.

Singer et al. do not disclose that the compositions contain a salt of a non-acidic cation and the anion of a mineral acid. However, the Examiner refers to (1) Satzinger et

al., which disclose that gabapentin can form pharmacologically compatible salts with inorganic and organic acids such as hydrochloric acid, sulfuric acid, phosphoric acid. Additionally, gabapentin can form salts from alkali metal or alkaline earth metals such as sodium, potassium, magnesium or calcium or even from quaternary ammonium groups, e.g. a tetramethyl-ammonium group (please see col. 2, lines 1-12) and (2) Jennings et al., which disclose pharmaceutical acid addition salts of gabapentin including salts derived from inorganic acids such as hydrobromic, nitric and hydroiodic acid, aliphatic sulfonic acids. Jennings et al also teach base addition salts formed with alkali and alkaline earth metals, wherein the base addition salts are formed by contacting the free acid from of the acidic compounds with a sufficient amount of base. (please see col. 2, lines 29-31; col. 7, lines 48-56; col. 8, lines 12-26).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the gabapentin compositions of Singer et al. to form base addition salts such as those described by Satzinger et al. and Jennings et al. because both Satzinger and Jennings clearly suggest that base addition salts of gabapentin are pharmaceutically or pharmacologically acceptable, and one of ordinary skill in the art would reasonably expect the resulting compositions to be equally effective in providing therapeutic benefit to patients in need of gabapentin. In other words, such a modification would have been motivated by the reasonable expectation of producing pharmaceutical compositions, which are just as therapeutically effective as the gabapentin compositions of Singer et al.

With respect to the specific amount (ppm) of the anion of the mineral acid, since Singer et al. establish that stability is dependent upon the amount of the anion of the mineral acid in the gabapentin composition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the amount of anion such that it is effective to optimize the stability of the overall gabapentin composition.

6. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Singer et al. in view of Satzinger et al. and Jennings et al. as applied to claims 19-28, 30-37 above, and further in view of Augart et al.

Singer, Satzinger, Jennings as applied above.

However, Singer, Satzinger and Jennings do not disclose that there is at most 5 ppm of one or more an acid addition salt of gabapentin. Yet, the Examiner refers to Augart et al., which discloses a pharmaceutical composition containing gabapentin hydrochloride (i.e. the acid addition salt of gabapentin) in combination with a pharmaceutically acceptable carrier. In order to keep undesirable lactam content of the composition low (i.e. not exceed 0.5% by weight of gabapentin lactam), and in order to ensure storage stability, Augart et al. teach that the composition should contain a proportion of hydrochloride, which does not exceed 20 ppm. This also applies to other mineral acids. Please see col. 1, lines 10-25; col. 2, lines 12-16; col. 3, lines 62-65; col. 5, lines 18-29, lines 11-17; Example 1.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the compositions of Singer, Satzinger and

Jennings to form an acid addition salt in a range of 5 ppm or less because Augart et al. establish that the amount of hydrochloride should not exceed 20 ppm, and one of ordinary skill in the art would reasonably expect a composition containing any amount below 20 ppm (such as the claimed 5 ppm or less) to be equally stable and to not contain more than 0.5% by weight gabepentin lactam. Finally, since Augart et al. establish that stability is dependent upon the amount (ppm) of hydrochloride in the gabapentin composition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the amount of hydrochloride as well as other acid addition salts such that it is effective to optimize the stability of the overall composition.

Conclusion

Claims 1-37 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 703-306-3227. The examiner can normally be reached on Mon-Fri. from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725 The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM

Nov. 16, 2003

Cybille Delacroix-Muirheid
Patent Examiner Group 1600